REMARKS

The specification has been amended in order to update the cross-reference to related application information.

Claims 2-4, 6, 8-10, 12-15 and 18 are amended for more proper antecedent basis; claim 4 is amended to add hyphenation as suggested by the Examiner; claims 7 and 11 are amended to improve syntax as suggested by the Examiner; claim 14 is amended to improve grammar as suggested by the Examiner; claims 3, 4, 9 and 13 are amended to excise language alleged to be unclear; claims 7 and 17 are amended to feature correcting IL-4 deficiency; claims 7, 11 and 17 are amended to feature acknowledged enabled subject matter; and claims 20 and 21 are added. Claims 2-4, 6-10, 12-15 and 17-21 are pending. Support for the amended claims and new claims 20 and 21 can be found in the previous claims and in the specification, for example at the paragraph bridging pages 3 and 4, page 4; second and third paragraphs; and at page5, fourth paragraph. No issue of new matter arises.

Specification

The Specification is amended to reference the patent number of the parent application.

Claim Objections

1-3. Claims 4, 7, 11 and 14 are amended in accordance with the Examiner's suggestions. Reconsideration and withdrawal of the corresponding objections are respectfully requested.

4. Claims 2-4 were objected to as allegedly being substantial duplicates of claim 17. Applicants respectfully traverse this objection.

Claim 2 further limits claim 17 by featuring a limitation relating to Th2 cells.

Claim 3 further limits claim 17 by featuring a limitation relating to T cells with sub-type HSA^{-}, $CD4^{-}CD8^{-}$ or $CD4^{+}CD8^{-}$, $CD44^{+}$, TCR-$\alpha\beta^{+}$, $V\beta8^{+}$, $NK1.1^{+}$.

Claim 4 further limits claim 17 by featuring a limitation relating to listed autoimmune diseases.

Thus each of claims 2-4 cannot properly be said to be a substantial duplicate of claim 17 from which each depends. Reconsideration and withdrawal of this objection are respectfully requested.

5. Claims 7-9 were objected to as allegedly being substantial duplicates of claim 11. Applicants respectfully traverse this objection.

Claim 11 recites: "A process for producing a pharmaceutical composition . . ." [emphasis added], whereas claims 7-9 feature chemical compositions *per se*. Thus claims 7-9 cannot properly be considered substantial duplicates of claim 11. Reconsideration and withdrawal of this objection are respectfully requested.

6. Claims 12-13 were objected to as allegedly being substantial duplicates of claim 14. Applicants respectfully traverse this objection.

Claim 12 features a process for producing a pharmaceutical composition for treating an autoimmune disease wherein the autoimmune disease is generated by a failure in the production of IL-4 by Th2 cells.

Claim 13 features a process for producing a pharmaceutical composition for treating an autoimmune disease wherein the autoimmune disease is generated by a failure in IL-4 production connected with a deficiency of T cells with sub-type HSA^-, $CD4^-CD8^-$ or $CD4^+CD8^-$, $CD44^+$, TCR-$\alpha\beta^+$, $V\beta8^+$, $NK1.1^+$.

Claim 14 features a process for producing a pharmaceutical composition for treating an autoimmune disease wherein the autoimmune disease is insulin-dependent diabetes mellitus.

These claims are not substantial duplicates. For example, depending on etiology, certain considerations might arise due to dependence of composition on the manner used to produce it. A specific process might for example result in added sugar, a characteristic that one might want to avoid for treating diabetes mellitus. TO give a specific example, claim 11, from which each of these claims depends, features a pharmaceutically acceptable vehicle or diluent. The vehicle or diluent mixed according

to claim 11 might be acceptable where failure in IL-4 production is connected with a deficiency of T cells with sub-type HSA^-, $CD4^-CD8^-$ or $CD4^+CD8^-$, $CD44^+$, TCR-$\alpha\beta^+$, $V\beta8^+$, $NK1.1^+$, (claim 13) but might not be acceptable where disease is insulin-dependent diabetes mellitus (claim 14). Thus each of claims 12 and 13 cannot properly be considered substantial duplicates of claim 14. Reconsideration and withdrawal of this objection are respectfully requested.

Rejection under 35 U.S.C. §112, first paragraph - enablement

Claims 2-4, 6-15 and 17-19 were rejected under 35 U.S.C. §112 as allegedly lacking enablement. The Office Action acknowledged that the specification was enabling for treating diabetes mellitus, pharmaceutical compositions, or a process for producing pharmaceutical compositions comprising T-cells incubated with IL-7, wherein the T-cells are thymocytes. Claims 7, 11 and 17 are amended above to include autoimmune diseases that arise from failure of immunoregulation by $CD4^+$ cells or failure of production of IL-4. Claims 7, 11 and 17 are also amended to recite autoimmune diseases related to diminished IL-4 production to correspond to other amendments to the claims. In view of these amendments reconsideration and withdrawal of this rejection are respectfully requested.

Rejections under 35 U.S.C. §112, second paragraph

1. Claims 2-4, 6-15 and 17-19 were rejected as allegedly omitting an essential step. The alleged omitted step is "an intended effect on the phenotype or function of the T-lymphocytes." However, the Office Action then questions whether the claimed method depends on T-lymphocytes acquiring a particular phenotype or biological function. The claims are alleged to lack a conclusion step. Applicants respectfully traverse this rejection.

Since claims 7-10 are composition of matter claims with no "steps" recited, this rejection cannot properly be said to be applicable with reference to omitted steps. With respect to this rejection in general, Applicants respectfully submit that their experiments show the effect of incubating lymphocytes in the presence of IL-7 gives

desired results. Knowledge of which specific characteristics stemming from such incubation is not essential to practicing the invention.

Claims rightfully are not required to recite all effects of a particular claimed action. The precise mechanism need not be known to achieve the preset invention. If the mechanism does not have to be known, it would be improper to require recitation in the claims. Reconsideration and withdrawal of this rejection are respectfully requested.

2. Claims 3, 9 and 13 were alleged to be unclear in reciting the phrase "quantitative and functional deficiency". Applicants have amended the claims to obviate this rejection. Reconsideration and withdrawal of this rejection are respectfully requested.

3. Claim 4 was alleged to be indefinite with respect to a "mechanism" as a disease. Claim 4 is amended to obviate this rejection. Reconsideration and withdrawal of this rejection are respectfully requested.

Rejections under 35 U.S.C. §102

1. Claims 2-4, 15 and 17 were rejected under 35 U.S.C. §102(e) over Grabstein. Applicants respectfully submit that the claims as amended above feature an end point of increased IL-4 production. Nowhere does Grabstein teach or require such an effect or result. Stimulating an immune response by monocytes/macrophages does not necessarily meet all the limitations of the present claims Since the claim amendments now distinguish over the cited reference, the rejection is obviated. Reconsideration and withdrawal of this rejection are respectfully requested.

2. Claims 2-4, 15 and 17 were rejected under 35 U.S.C. §102 over Williams. Applicants respectfully submit that the claims as amended above feature an end point of increased IL-4 production. Nowhere does Williams teach or require such an effect or result. Affecting platelet production does not necessarily meet all the limitations of the present claims. Since the claim amendments now distinguish over the cited reference, the rejection is obviated. Reconsideration and withdrawal of this rejection are respectfully requested.

Rejection under 35 U.S.C. §103

Claims 2, 3, 6-15 and 17-19 were rejected under 35 U.S.C. §103 over Gombert in view of Jicha. Applicants respectfully traverse this rejection. The Gombert reference is not properly cited as prior art against the present application. Applicants attach a copy of the International Search Report indicating that Gombert is published after the claimed priority date. See page 3, the "P,X" notation for the third reference. Because of this, this reference is not properly cited in a prior art rejection, for example under 35 U.S.C. §102(b).

Furthermore, both Marc Gombert and Andre Herbelin are authors of the cited reference and inventors listed on the present patent application. Applicants respectfully submit that citation of Gombert as a 35 U.S.C. §102(a) reference is improper as the reference is not evidence of invention by another. For at least these reasons, Applicants respectfully submit that the rejection under 35 U.S.C. §103 is improper. Reconsideration and withdrawal of this rejection are respectfully requested.

Obviousness-type double patenting rejection

1 and 2. Applicants acknowledge the obviousness-type double patenting rejections. However, since the present application has no indicated allowable subject matter, it would be premature to require a terminal disclaimer when other actions, for example an amendment to the claims that would invoke 35 U.S.C. §121, might obviate the requirement. Applicants will consider amendment or filing a terminal disclaimer when allowable subject matter is indicated.

Added claims

Claims 20 and 21 are added. These claims are similar to claim 17 but do not feature administration of IL-7. They feature administration of IL-7 treated cells, one of the alternatives recited in claim 17. Applicants respectfully submit that none of the applied references teach these limitations.

Conclusion

In view of the above amendments and remarks, Applicants respectfully request reconsideration and withdrawal of all pending objections and rejections. Applicants respectfully submit that the application is now in condition for allowance and request prompt issuance of a Notice of Allowance. Should the Examiner believe that anything further is desirable that might put the application in even better condition for allowance, the Examiner is requested to contact the undersigned at the telephone number listed below.

Fees

No fees not otherwise provided for are believed to be necessitated by the instant response. However, should this be in error, authorization is hereby given to charge Deposit Account No. 18-1982 for any underpayment, or to credit any overpayments.

Respectfully submitted,

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sanofi aventis Docket No. IVD938 US DIV

INTERNATIONAL SEARCH REPORT

Interna al Application No
PCT/FR 97/00343

A. CLASSIFICATION OF SUBJECT MATTER
IPC 6 A61K38/20 A61K35/14

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)
IPC 6 C07K A61K

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	WO 92 01459 A (IMMUNEX CORP) 6 February 1992 cited in the application see page 4, line 9 - line 23 ---	7-14
X	FASEB JOURNAL, vol. 4, no. 7, 1990, page A2183 XP002019544 LYNCH ET AL: "IL-7 INDUCES LAK ACTIVITY IN RESTING MURINE T CELLS" * abstract 2823 * ---	7-14
X	WO 96 01122 A (DANA FARBER CANCER INST INC) 18 January 1996 see page 2, line 6 - page 3, line 6 --- -/--	7-14

[X] Further documents are listed in the continuation of box C.

[X] Patent family members are listed in annex.

* Special categories of cited documents :

"A" document defining the general state of the art which is not considered to be of particular relevance

"E" earlier document but published on or after the international filing date

"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)

"O" document referring to an oral disclosure, use, exhibition or other means

"P" document published prior to the international filing date but later than the priority date claimed

"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.

"&" document member of the same patent family

Date of the actual completion of the international search	Date of mailing of the international search report
12 June 1997	23.06.97

Name and mailing address of the ISA	Authorized officer
European Patent Office, P.B. 5818 Patentlaan 2 NL - 2280 HV Rijswijk Tel. (+ 31-70) 340-2040, Tx. 31 651 epo nl, Fax (+ 31-70) 340-3016	Sitch, W

Form PCT/ISA/210 (second sheet) (July 1992)

C.(suite) DOCUMENTS CONSIDERES COMME PERTINENTS

Catégorie *	Identification des documents cités, avec, le cas échéant, l'indication des passages pertinents	no. des revendications visées
A	DATABASE MEDLINE FILE SERVER STN KARLSRUHE ABRÉGÉ 94101260, COSTELLO ET AL: "THE PLEIOTROPIC EFFECTS OF INTERLEUKIN 7 AND THEIR PATHOLOGIC AND THERAPEUTIC IMPLICATIONS" XP002019546 & EUROPEAN JOURNAL OF MEDICINE, (1992 MAY) 1 (2) 119-21 voir abrégé ---	
A	IMMUNOLOGY, vol. 80, no. 3, 1 Novembre 1993, pages 451-457, XP000560404 COSTELLO R ET AL: "INTERLEUKIN-7 IS A POTENT CO-STIMULUS OF THE ADHESION PATHWAY INVOLVING CD2 AND CD28 MOLECULES" * page 451,abrégé * ---	
A	J.IMMUNOL., vol. 155, 1995, pages 4544-4550, XP002019545 DO CARMO LEITE-DE-MORAES ET AL: "MHC CLASS I-SELECTED CD4-CD8-TCR-ALPHABETA+ T CELLS ARE A POTENTIAL SOURCE OF IL-4 DURING PRIMARY IMMUNE RESPONSE" cité dans la demande * page 4544,abrégé * ---	
A	J.EXP.MED., vol. 178, 1993, pages 87-99, XP000610471 RAPOPORT ET AL: "INTERLEUKIN 4 REVERSES T CELL PROLIFERATIVE UNRESPONSIVENESS AND PREVENTS THE ONSET OF DIABETES IN NONOBESE DIABETIC MICE" cité dans la demande * page 87,abrégé * ---	
A	J.EXP.MED., vol. 178, 1993, pages 901-908, XP000611517 BIX ET AL: "POSITIVE SELECTION OF VBETA8+CD4-8- THYMOCYTES BY CLASS I MOLECULES EXPRESSED BY HEMATOPOIETIC CELLS" cité dans la demande * page 901,abrégé * --- -/--	

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INTERNATIONAL SEARCH REPORT

Interna al Application No
PCT/FR 97/00343

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	J.EXP.MED., vol. 180, 1994, pages 653-661, XP000611515 VICARI ET AL: * INTERLEUKIN 7 INDUCES PREFERENTIAL EXPANSION OF VBETA8.2+CD4-8- AND VBETA8.2+CD4+8- MURINE THYMOCYTES POSITIVELY SELECTED BY CLASS I MOLECULES" cited in the application * page 653,abstract * ---	
A	AUTOIMMUNITY, vol. 15, 1993, pages 113-122, XP000610469 ANDERSON ET AL: "INSULIN-DEPENDENT DIABETES IN THE NOD MOUSE MODEL II. BETA CELL DESTRUCTION IN AUTOIMMUNE DIABETES IS A TH2 AND NOT A TH1 MEDIATED EVENT" cited in the application * page 113,abstract * ---	
P,X	C.R.ACAD.SCI.PARIS,SCIENCES DE LA VIE/LIFE SCIENCES, vol. 319, February 1996, pages 125-129, XP000608939 GOMBERT ET AL: "EARLY DEFECT OF IMMUNOREGULATORY T CELLS IN AUTOIMMUNE DIABETES" see the whole document ---	1-16
P,X	INTERNATIONAL IMMUNOLOGY, vol. 8, no. 11, November 1996, pages 1751-1758, XP000674709 GOMBERT ET AL: "IL-7 REVERSES NK1+ T CELL-DEFECTIVE IL-4 PRODUCTION IN THE NON-OBESE DIABETIC MOUSE" see the whole document -----	1-16